

Tumor Markers and Alcohol Consumption

TÜMÖR MARKIRLARI VE ALKOL TÜKETİMİ

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Summary

Purpose: To find out whether tumor markers were useful to determine if there were some organs affected by alcohol.

Instution: Selçuk University, Faculty of Medicine, Dept. of Biochemistry, Konya, Turkey.

Materials and Methods: Serum concentrations of the tumor markers were examined in 33 alcohol consumers aged between 20-48 (mean 35.3±6.3) and 36 non-consumer aged between 18-55 (mean 37.8±10.3). Serum alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA), prostate specific antigen (PSA), and carbohydrate antigen 19-9 (CA 19-9) levels were determined by using a solid-phase, two-site chemiluminescent enzyme immunometric assay. Routine methods were used for the measurement of aspartate aminotransferase (AST), alanine aminotransferase (ALT) and gamma-glutamyl transferase (GGT) activities.

Results: Significant elevation in AFP (p<0.05), CEA (p<0.05), AST (p<0.01), GGT (p<0.001) was found in alcohol drinkers as compared to non-drinkers. AFP and CEA were found to have been correlated positively with age and alcohol consumption years (p<0.05, for all). There was also a significant correlation between serum GGT activity and the amount of alcohol consumed (p<0.01).

Conclusion: The increase of AFP, CEA levels, and AST, GGT activities in alcohol drinkers may reflect alcohol-induced liver affection.

Key Words: Alpha-fetoprotein,
Carbohydrate antigen 19-9,
Carcinoembryonic antigen,
Prostate specific antigen, Alcohol

T Klin J Med Sci 2001, 21:49-53

Özet

Amaç: Bazı organların alkolden etkilenip etkilenmediğinin tesbitinde tümör markırlarının kullanılabilir kullanılmayacağını araştırmak.

Çalışmanın Yapıldığı Yer: Selçuk Üniversitesi Tıp Fakültesi Biyokimya Anabilim Dalı, Konya.

Materyal-Metod: Yaşları 20-48 (ortalama 35.3±6.3) arası olup alkol alan 33 kişi ve yaşları 18-55 (ortalama 37.8±10.3) arasında olup alkol almayan 36 kişide serum tümör markırları konsantrasyonları çalışıldı. Serum alfa-fetoprotein (AFP), karsinoembriyonik antijen (CEA), prostat spesifik antijen (PSA) ve karbonhidrat antijen 19-9 (CA-19-9) düzeyleri solid faz, two-site kemilüminesans enzim immunometric assay metodu kullanılarak ölçüldü. Serum alanin amino transferaz (ALT), aspartat amino transferaz (AST) ve gama-glutamil transferaz (GGT) düzeyleri rutin metodlarla belirlendi.

Bulgular: Alkol alanlarda almayanlarla karşılaştırıldığında AFP (p<0.05), CEA (p<0.05), AST (p<0.01) ve GGT (p<0.001) düzeyleri anlamlı olarak yüksek bulundu. AFP ve CEA yaşla ve alkol kullanma süresiyle pozitif korelasyon gösterdi (p<0.05, hepsi için). Ayrıca tüketilen alkol miktarı ile GGT düzeyleri arasında da anlamlı korelasyon tesbit edildi (p<0.01).

Sonuç: AFP ve CEA düzeyleriyle AST ve GGT aktivitelerindeki artış alkolün indüklediği karaciğer hasarını yansıtabilir.

Anahtar Kelimeler: Alfa-fetoprotein,
Karbonhidrat antijen 19-9,
Karsinoembriyonik antijen,
Prostat spesifik antijen, Alkol

T Klin Tıp Bilimleri 2001, 21:49-53

Geliş Tarihi: 28.03.2000

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Human cancer is the second leading cause of death in the industrialized world (1). Cancer prevention efforts and the detection of asymptomatic cancer are considered to be major interventions that can influence cancer incidence, complications, and mortality.

The fact that certain neoplasms may exist in the organism for many years without expressing detectable signs of malignancy has been known to clinicians for some years. Unfortunately, in most cases, the clinical detection of cancer doesn't occur when the patient is asymptomatic. Physical examinations, X-rays, and routine laboratory evaluations are used in the early detection of cancer. In certain types of cancer, some biochemical or biological markers are used. This brings us to the field of "tumor markers" (2). The term usually refers to substances, which are present in tumor or produced by a tumor or the tumor's host in response to the tumor's presence. These markers can be used to differentiate a tumor from normal tissue or to determine the presence of a tumor based on measurement in the blood or secretions. Such substances can be found in cells, tissues, or body fluids and measured to determine the presence of cancer (3).

Some tumor marker levels elevate in some malignancies. For example, alpha-fetoprotein (AFP) is a marker for hepatocellular and germ cell carcinoma (4). Carcinoembryonic antigen (CEA) can be elevated in patients with colorectal, gastrointestinal, lung and breast carcinoma (3). Prostate specific antigen (PSA) is the most valuable currently identified serum marker for carcinoma of the prostate (5). Carbohydrate antigen 19-9 (CA 19-9) is a marker for colorectal and pancreatic carcinoma (6).

It is now well known that a number of factors in our environment are related to the development of cancer. Factors well identified include tobacco use, which is estimated to cause 30% of all deaths from cancer. Viruses and geophysical agents represent 6%, and a small percentage are due to occupation-related exposure to carcinogens. Concerning dietary factors, the estimation is 30%, ranging from 10% to 50% (2). Alcohol, widely consumed, is one of these factors. Clinically, an association between heavy drinking and certain types of cancer has been observed for many years (7-12). In a study, heavy drinkers were found to have roughly a 10-fold increased risk of developing cancer of the mouth (9). An increased incidence of esophageal cancer has been described in the alcoholics (10). Hepatocellular carcinoma also has been associated with alcoholism. It is showed that heavy drinking

enhances the development of hepatocellular carcinoma (11,12). The purpose of the study was to find out whether tumor markers were useful to determine if there were some organs affected by alcohol.

Materials and Methods

The study group (SG) and the control group (CG) consisted of 33 alcohol drinkers and 36 healthy non-drinkers, respectively, and all subjects were men. The mean ages of SG and CG were 35.3 ± 6.3 (min, max: 20,48) and 37.8 ± 10.3 (min,max: 18,55), respectively. The mean amount of alcohol consumed was 139.35 ± 123.54 g/day (min,max: 20,550) in SG. The people in SG had been drinking for 15.04 ± 7.99 years (min,max: 4,32). None of CG was drinker. Apart from two subjects in CG, all subjects in both groups were smokers. The periods of smoking were 13.0 ± 9.1 years and 10.3 ± 6.4 years in SG and CG, respectively. It had been smoked 0.7 ± 0.4 pack and 0.5 ± 0.3 pack per day in SG and CG, respectively.

All subjects were of normal nutritional status. They had no clinical complaints and findings. Routine blood count and liver function tests (AST, ALT, bilirubins and proteins) were performed and there was no significant difference between the groups. The amount of alcohol consumed was calculated according to the information provided by the drinkers. For this purpose, firstly the types and the amounts of drinkings, which were consumed by drinkers per day, were obtained. Then, the amount of alcohol were calculated according to alcohol contents of each type of drinking. SG were selected from regular drinkers and their blood was drawn regardless of their being fast when they were at pubs and restaurants. However, those who hadn't had alcohol within at least eight hours were included in the study. After interviewing with each subject, a total of 10 ml of venous blood was drawn. The serum from the samples was separated and all assays were performed daily.

Serum AFP, CEA, PSA and CA 19-9 levels were determined by using a solid-phase, two-side chemiluminescent enzyme immunometric assay (Immulite Automated Analyzer, DPC, US). The activities of AST, ALT, and GGT were measured by commercially available kits (Bayer, US) by using an autoanalyser (Technicon RA-XT, Bayer, US).

Table 1. Comparison of parameters of the study and the control groups.

Parameters	Study group	Control group
	Mean (SD) n=33	Mean (SD) n=36
AFP (ng/ml)	1.97 (1.34)	1.37 (0.58)*
CEA (ng/ml)	3.12 (0.75)	2.67 (0.87)*
PSA (ng/ml)	1.06 (0.61)	0.97 (0.59)
CA 19-9 (U/ml)	10.56 (6.01)	11.04 (4.49)
AST (U/L)	31.60 (17.91)	22.01 (7.30)**
ALT (U/L)	29.06 (16.09)	26.84 (17.37)
GGT (U/L)	74.91 (73.22)	31.13 (17.53)***
*	p<0.05	
**	p<0.01	
***	p<0.001	

The kits were based on generally accepted enzymatic methods.

All values were expressed as mean±standard deviation. SPSS for Windows 6.0 was used for statistical analysis. Student's t-test and the Pearson correlation test were used when appropriate. The differences were considered to be significant when the probability was less than 0.05.

Results

Comparisons of parameters of the SG and the CG are given Table 1.

As seen from Table 1, significant elevation in AFP (p=0.024), CEA (p=0.027), AST (p=0.006), and GGT (p=0.001) were found in SG as compared to controls. AFP and CEA were found to be correlated positively with age (p=0.046, r=0.4510, p=0.033, r=0.4771, respectively) and alcohol consumption years (p=0.039, r=0.4646, p=0.043, r=0.4561, respectively). There was also a significant (p=0.006, r=9.4842) correlation between serum GGT activity and the amount of alcohol consumed.

Discussion

A relationship between circulating quantifiable tumor markers and a patient's tumor burden and disease activity has been noted since the 1930s (13). Since then, a large number of serum tumor markers have been identified, but few are clinically useful as adjuncts in cancer detection, diagnosis, prognosis, and monitoring the patient's response to

therapy (14). When measurable serum levels of CEA were first described in 1965, it was anticipated that this marker might prove to be a highly effective management tool for patients with lung, breast, and GI cancers (15). Unfortunately, its current role in the clinical care of these tumors has been found to be much more limited than initially expected (16). More specifically, measurements of CEA are not useful in screening for cancer or for establishing a definitive diagnosis of cancer (17). However, it can be used successfully as a diagnostic and prognostic adjunct and for therapeutic monitoring (18). CEA is still a useful tumor marker for medullary carcinoma of thyroid, and it is detectable only in thyroid tumors originating from C cells (19).

Serum CEA levels are influenced by alcohol, smoking, renal function, liver disease, and other nonmalignant GI disorders (15,20,21). In most studies, CEA concentrations up to 5 ng/ml were regarded as normal if individuals were mostly nicotine and alcohol addicts (22). Herbeth et al. showed significant association between CEA levels higher than 2.5 ng/ml and both age and alcohol consumption (23). These findings are in accordance with ours that CEA elevated significantly in SG and correlated significantly age and alcohol consumption years.

Although CEA is not a specific test as a tumor marker, according to the findings in the study, it may be thought that elevated CEA level may be due to alcohol. One of the findings is that SG consisted of people without clinical complaints and findings and their CEA levels were higher as compared to CG. Another finding is that there was a positive correlation between CEA and alcohol consumption years. However, apart from two subjects in SG, the fact that all subjects were smokers shows that smoking does not account for elevated CEA level.

AFP is a well-established tumor marker for hepatocellular carcinoma and germ cell tumors (4,24). An elevated serum concentration of AFP has been reported in viral hepatitis, metabolic and hereditary diseases, some cases of cirrhosis, and alcoholic liver disease (25-27).

Detailed evidence has been presented for the increased incidence of cancer of the upper alimentary tract and the colon in the alcoholic (9).

Hepatocellular carcinoma has also been associated with alcoholism. However, this has usually been attributed not to ethanol but rather to the ensuing cirrhosis. Recently, some clinical evidence has accumulated that, even in the absence of cirrhosis, hepatocellular carcinoma of the liver is linked to alcoholism (9).

Several studies of AFP, albeit with different assay methods, have been performed in alcoholic liver disease, and most studies report the finding of occasionally elevated AFP (25,28). These confirm our findings. However, in one study, it was found that there was a lower concentration of AFP in most patient with alcoholic liver disease and a negative correlation between AFP and the extent of clinical, biochemical and histological signs of disease (27).

The positive correlation of AFP with age in adults has previously been noted, and this confirms the study (29). On the other hand, Bayati et al. showed that there was no significant difference in serum AFP based on alcohol consumption (30). Although no clinical findings were found for liver disease in SG, the probability of liver disease cannot be excluded, because liver biopsy was not performed. On the other hand, the fact that increased GGT and AST activities in SG, which are more specific to alcoholic liver disease, and the significant correlation between GGT and alcohol consumed shows that liver was affected by alcohol. Christiansen et al. found that AFP increased significantly in alcohol drinkers, and it decreased after withdrawal from alcohol (26). This supports our findings. The liver affection in turn gives a reduced catabolism of glycoproteins, i.e. most tumor markers. This is the most probable explanation for the elevation of CEA and AFP.

No increase in PSA, highly specific for prostate carcinoma, was found, and there is no evidence between alcohol and both PSA and prostate carcinoma.

CA 19-9 elevates in some pancreas and colon malignancies (6). Traverso et al. reported that history of alcohol abuse was significantly associated with pancreas malignancy (31). Chalasani et al. showed that alcohol consumption was significantly associated with cholangiocarcinoma (32). Chen et al. also noted that uncontrolled regeneration or neoplasia was common in pancreas of the alcoholic

(33). As mentioned, colon and pancreas were affected by alcohol.

As a result it can be concluded that because of the fact that no increase was found in PSA and CA 19-9 in SG, these markers are not useful for early detection of if these organs were affected by alcohol. It can also be thought that liver affected by alcohol may account for increased CEA and AFP levels.

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